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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,602	05/04/2001	Yao-Tseng Chen	L0461/7105(JRV/MXA)	8884

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EXAMINER	
LY, CHEYNE D	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 11/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/849,602	CHEN ET AL.	
	Examin r	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4, 6,15,16, 20, 47,48,51, 56, 57, 60, 86-90 and 98* is/are pending in the application.

4a) Of the above claim(s) *6,20,51,56,57,60 and 90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,15,16,47,48,86-89, and 98* is/are rejected.

7)☒ Claim(s) *1-4, 15, 16, 47, 48, 86-89, and 98* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' arguments filed July 18, 2003 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

OBJECTIONS

2. Claims 1-4, 15, 16, 47, 48, 86-89, and 98 are objected to due to the inclusion of subject matter, which has been non-elected due to a restriction requirement and therefore, the non-elected subject matter (SEQ ID NO. 2-4 and 6-10) has been withdrawn from consideration.

CLAIM REJECTIONS - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 15, 16, and 98 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. This rejection is maintained with respect to claims 15, 16, and 98, as recited in the previous office action mailed April 15, 2003.

4. Specific to claims 15 and 98, the active steps for determining onset, progression, or regression, of cancer in a subject causes the claim to be vague and indefinite. Line 3 is directed to the step of "obtaining from a subject a first biological sample" for analysis and line 9 is

directed to the step of "obtaining from a subject a second biological sample" for analysis. One interpretation of these two steps is that samples are obtained from different subjects. How is the "determining onset, progression, or regression, of cancer" achieved when one maybe comparing samples from different subjects? Applicant can resolve this issue by particularly pointing out that the samples are obtained from the same subject. Clarification of the metes and bounds of the instant claim is required. Claim 16 is reject for being dependent from claim 15.

LACK OF UTILITY UNDER 35 U.S.C. § 101:

5. The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

6. The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

7. Claims 1-4, 15, 16, 47, 48, 86-89 and 98 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

8. The critical limitations of claims 1-4, 15, 16, 47, 48, 86-89 and 98 are nucleic acids, SEQ ID NOs: 1 and 5 encoding polypeptides, SEQ ID NOs: 16 and 20.

9. This rejection is maintained with respect to claims 1-4, 15, 16, 47, 48, 86-89 and 98, as recited in the previous office action mailed April 15, 2003.

RESPONSE TO APPLICANT'S ARGUMENT

10. Applicant argues the claimed invention is directed to the nucleic acid molecules and polypeptides for diagnosis of colon cancer and/or assessment of treatment of colon cancer in a subject. The claimed invention is supported by a substantial utility due to said nucleic acid molecules encode polypeptides recognized by antibodies in the sera of individuals with colon cancer "known by virtue of the method by which the nucleic acid molecules were isolated (SEREX)." Further, "the polypeptides encoded by these nucleic acid molecules are not recognized by the immune systems of the normal individuals tested, but are recognized by the immune systems of persons having colon cancer". Applicant's arguments have been fully considered and found to be unpersuasive as discussed below.

11. Specific to the argument of the claimed nucleic acid sequences having been isolated and identified by the SEREX method. The said argument is found to be unpersuasive because said

SEREX method requires antigen to be identified via sequence comparisons with either the EMBL or GenBank databases "Sequence alignments were performed with DNAIS (Pharmacia) and BLAST software on European Molecular Biology Laboratory (EMBL) and GenBank databases (Sahin et al., Page 11810, column 2, lines 41-44 to Page 11811, column 1, lines 1-7). It is acknowledged that "the polypeptides encoded by these nucleic acid molecules are not recognized by the immune systems of the normal individuals tested, but are recognized by the immune systems of persons having colon cancer" (Table 1). Due to the SEREX method relying solely on sequence homology for identifying said polypeptides as colon cancer antigens (Sahin et al., page 11812, column 2, lines 23-26), it is well known in the art that one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject matter would be the same as that of the similar sequence without being presented with factual evidence.

12. It is re-iterated that the claimed polynucleotides are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, a nucleic acid may be utilized to obtain a protein. The protein could then be used in conducting research to functionally characterize the protein. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case, the protein produced as a final product resulting from processes involving the nucleic acid does not have asserted or identified specific and substantial utilities. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved, such as the cancer-associated

polypeptide encoded by SEQ ID NOs:1 and 5, does not define a "real world" context for use. Similarly, the other listed utilities and asserted utilities as summarized in the instant specification (Pages 23-24) are not substantial due to being generic in nature and applicable to many such compounds.

13. It is acknowledged that Applicants disclose colon cancer-associated polypeptides, which have been identified through SEREX screening of patients with cancer (Page 13, lines 10 and 11). As disclosed in the Sahin et al. reference cited in this instant application, the process of identifying antigen is through sequence analysis. "Sequence alignments were performed with DNAIS (Pharmacia) and BLAST software on European Molecular Biology Laboratory (EMBL) and GenBank databases (Sahin et al., Page 11810, column 2, lines 41-44 to Page 11811, column 1, lines 1-7). The colon cancer-associated polypeptides of this instant application have been identified through SEREX screening of patients with cancer. The SEREX method requires antigen to be identified via sequence comparisons with either the EMBL or GenBank databases Absent factual evidence, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject matter would be the same as that of the similar sequence.

14. Furthermore, it is unclear whether the similar sequence identified in the prior art (EMBL or GenBank databases) has actually been tested for the biological activity or whether this also is an asserted biological activity based upon sequence similarity to yet a different sequence. Note that it would have been well known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been well known that even a single nucleotide

or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Lopez et al. (Molecular Biology, 32:881-891,1999); Attwood (Science, 290:471-473, 2000); Gerhold et al. (BioEssays, 18(12):973-981, 1996); Wells et al. (Journal of Leukocyte Biology, 61(5):545-550, 1997); and Russell et al. (Journal of Molecular Biology, 244:332-350, 1994). However, this level of factual evidence is absent here.

Claims Rejected Under U.S.C. § 112, First Paragraph

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF ENABLEMENT

16. Claims 1-4, 15, 16, 47, 48, 86-89 and 98 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

17. This rejection is maintained with respect to claims 1-4, 15, 16, 47, 48, 86-89 and 98, as recited in the previous office action mailed April 15, 2003.

18. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

RESPONSE TO APPLICANT'S ARGUMENT

19. Applicant argues that the examiner does not present sufficient support for the above lack of enablement rejection. The said argument has been fully considered and found to be unpersuasive due to said applicant has not disclosed how to use the invention due to the lack of a substantial utility (MPEP §2107 (II)).

20. It is re-iterated that the claimed invention is not supported by a substantial utility for the reasons set forth above (refer to 35 U.S.C. § 101 rejection), one skilled in the art would not know how to use the claimed invention without undue experimentation.

CONCLUSION

21. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

22. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

23. This application contains claims 6, 20, 51, 56, 57, 60, and 90 drawn to an invention nonelected with traverse in a previous action mailed February 21, 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

24. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

26. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

27. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
10/28/03